Agamree (vamorolone), Emflaza (deflazacort) Prior Authorization with Quantity Limit Program Summary

This program applies to MN Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
07-01-2024	08-01-2017

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Agamree® (vamorolone) Oral suspension	Treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older		6
Emflaza® (deflazacort) Tablet* Oral suspension	Treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older	* Generic available	1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Duchenne Muscular Dystrophy	Duchenne muscular dystrophy (DMD) is a genetic disorder characterized by progressive muscle degeneration and weakness due to the alterations of a protein called dystrophin that helps keep muscle cells intact. DMD is the most common childhood form of muscular dystrophy as well as the most prevalent of the muscular dystrophies. DMD is an X-linked recessive inherited genetic condition primarily affecting males, although females who carry the defective gene may show some symptoms. Prevalence is 15.9 per 100,000 live male births in the US and 19.5 per 100,000 live male births in the UK. Dystrophin is the protein associated with this affected gene and provides structural stability to skeletal muscles. Mutations in this gene, and subsequent lack of dystrophin in muscle fiber, result in a rapidly progressing disease involving muscle degeneration and weakness. Symptom onset is in early childhood and many children lose the ability to walk by early adolescence. Beyond muscle weakness, other symptoms include enlargement of the calf muscles, lumbar lordosis, and later on cardiomyopathy and poor respiratory function. Until relatively recently, boys with DMD usually did not survive much beyond their teen years. Thanks to advances in cardiac and respiratory care, life expectancy is increasing and many young adults with DMD are surviving into their early 30s. Currently, there is no cure for DMD, and therapies are supportive in nature. Physical therapy, occupational therapy, respiratory care, speech therapy, braces/wheelchairs/contractures and glucocorticoid therapy are among the most common therapies.(2-4) Corticosteroid

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	(glucocorticoids) are the standard of care for DMD, although they remain non-curative. Their use improves muscle strength, improves timed motor function, delays loss of ambulation, improves pulmonary function, reduces the need for scoliosis surgery, delays onset of cardiomyopathy, increases survival, and maintains quality of life. The choice of which glucocorticoid to use depends on cost, formulation, and perceived side-effect profiles.(3) The updated American Academy of Neurology practice guidelines concluded that prednisone and deflazacort are possibly equally effective for improving motor function in patients with DMD (2 Class III studies). There is insufficient evidence to directly compare the effectiveness of prednisone vs deflazacort in cardiac function in patients with DMD (1 Class III study of a combined cohort). The AAN states that deflazacort could be offered as an intervention for patients with DMD to improve strength and timed motor function and delay the age at loss of ambulation by 1.4–2.5 years (Level C), improve pulmonary function (Level C), reduce the need for scoliosis surgery (Level C), delay the onset of cardiomyopathy by 18 years of age (Level C), increase survival at 5 and 15 years of follow-up (Level C). Prednisone is possibly associated with greater weight gain in the first 12 months of treatment, with no significant difference in weight gain with longer-term use compared with deflazacort (2 Class III studies). Deflazacort is possibly associated with an increased risk of cataracts compared with prednisone, although most are not vision-impairing (2 Class III studies).(5) Vamorolone is a first-in-class anti-inflammatory steroidal drug that has shown to have dissociative properties. The structure of vamorolone is similar to other glucocorticoids: it binds to the glucocorticoid receptor and retains the anti-inflammatory effects characteristic of traditional steroids, preferentially inducing transrepression with little-to-no transactivation or cis-repression. Transrepression is the suppression of the pro-inflammatory nuclear factor kappa B (NF-κB) signaling pathway, to exert the well-known potent anti-inflammatory effects of steroids. By not inducing transactivation or cis-repression, vamorolone is purported to elicit fewer adverse effects. Vamorolone is also a mineralocorticoid receptor antagonist, and thus may have the potential to treat DMD-associated cardiomyopathy through modulation of blood pressure.(7)
Efficacy	**Emflaza** The effectiveness of Emflaza for the treatment of DMD was established in one multicenter, randomized, double-blind, placebo-controlled, 52-week study. 196 male patients between the ages of 5 and 15 years old with documented mutation of the dystrophin gene, onset of weakness before 5 years of age, and serum creatinine kinase activity at least 10 times the upper limit of normal at some stage in their illness were enrolled. Patients were randomized to receive Emflaza (0.9 or 1.2 mg/kg/day), an active comparator, or placebo. After 12 weeks, placebo patients were re-randomized to receive either Emflaza or the active comparator. All patients continued treatment for an additional 40 weeks. Efficacy was evaluated by assessing the change between Baseline and Week 12 in average strength of 18 muscle groups. The change in average muscle strength score between Baseline and Week 12 was significantly greater for the deflazacort 0.9 mg/kg/day dose group than for the placebo group. (p-value 0.017). Although not a pre-specified statistical analysis, compared with placebo, the deflazacort 0.9 mg/kg/day dose group demonstrated at Week 52 the persistence of the treatment effect observed at Week 12.(1) A 2nd study of a randomized, double-blind, placebo-controlled, 104-week clinical trial evaluated deflazacort in comparison to placebo. The study population consisted of 29 male children 6 to 12 years of age with a DMD diagnosis confirmed by the documented presence of abnormal dystrophin or a confirmed mutation of the dystrophin gene. The results of the analysis of the primary endpoint of average muscle strength scores in this 2nd study (graded on a 0-5 scale) at 2 years were not statistically significant, possibly because of a limited number of patients remaining in the placebo arm (subjects were discontinued from the trial when they lost ambulation). Although not

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	statistically controlled for multiple comparisons, average muscle strength scores at Months 6 and 12, as well as the average time to loss of ambulation, numerically favored deflazacort in comparison with placebo.(1) **Agamree** The effectiveness of Agamree for the treatment of DMD was evaluated in a multicenter, randomized, double-blind, parallel-group, placebo- and active-controlled, multinational 24-week study (Study 1; NCT03439670). The study randomized 121 male patients with DMD to one of the following treatment groups: AGAMREE 6 mg/kg/day (n=30), AGAMREE 2 mg/kg/day (n=30), prednisone 0.75 mg/kg/day (n=31), or placebo (n=30) for 24 weeks. After 24 weeks, patients on prednisone and placebo received either AGAMREE 6 mg/kg/day (n=29) or AGAMREE 2 mg/kg/day (n=29) for an additional 20 weeks. The study included patients 4 to less than 7 years of age at time of enrollment in the study who were corticosteroid naïve and ambulatory, with a confirmed diagnosis of DMD.(6) The primary endpoint was the change from baseline to Week 24 in Time to Stand Test (TTSTAND) velocity for AGAMREE 6 mg/kg/day compared to placebo. TTSTAND velocity is a measure of muscle function that measures the time required for the patient to stand to an erect position from a supine position (floor). The key secondary endpoints consisted of change from baseline to Week 24 in TTSTAND velocity (AGAMREE 2 mg/kg/day vs placebo), 6 Minute Walk Test (6MWT) distance (AGAMREE 6 mg/kg/day vs placebo and 2 mg/kg/day vs placebo) and Time to Run/Walk 10 meters (TTRW) velocity (AGAMREE 6 mg/kg/day vs placebo and 2 mg/kg/day vs placebo). The 6MWT measures the distance that a patient can walk on a flat, hard surface in a period of 6 minutes and TTRW measures the time that it takes a patient to run or walk 10 meters. The fixed sequential testing process was applied to the key secondary endpoints in the order listed above.(6) The primary endpoint and key secondary endpoints were met for the AGAMREE 6 mg/kg/day treatment group. The AGAMREE 2 mg/kg/day treatment group was statistically significant vs. placebo for TTSTAND and 6MWT, but was not statistically significant vs. placebo for TTRW.(6)
Safety	Emflaza is contraindicated in patients with known hypersensitivity to deflazacort or to any of the inactive ingredients. Instances of hypersensitivity, including anaphylaxis, have occurred in patients receiving corticosteroid therapy.(1) Agamree is contraindicated in patients with known hypersensitivity to vamorolone or to any of the inactive ingredients in Agamree.(6)

REFERENCES

Number	Reference
1	Emflaza prescribing information. Marathon Pharmaceuticals. June 2021.
2	Duchenne muscular dystrophy (DMD). Muscular Dystrophy Association. (2021, April 29). https://www.mda.org/disease/duchenne-muscular-dystrophy
3	Biggar, W. D., Skalsky, A., & McDonald, C. M. (2022). Comparing deflazacort and prednisone in Duchenne Muscular Dystrophy. Journal of Neuromuscular Diseases, 9(4), 463–476. https://doi.org/10.3233/jnd-210776
4	U.S. Department of Health and Human Services. Muscular dystrophy. National Institute of Neurological Disorders and Stroke. https://www.ninds.nih.gov/health-information/disorders/muscular-dystrophy

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Number	Reference
5	Gloss, D., Moxley, R. T., Ashwal, S., & Oskoui, M. (2016). Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy. Neurology, 86(5), 465–472. https://doi.org/10.1212/wnl.0000000000002337
6	Agamree prescribing information. Catalyst Pharmaceuticals. October 2023.
7	Kourakis, Stephanie, Timpani, Cara A., (2021). Standard of Care Versus New-Wave Corticosteroids in the Treatment of Duchenne Muscular Dystrophy: Can we Do Better? Orphanet Journal of Rare Diseases. 2021.16(1):117. DOI: 10.1186/s13023-021-01758-9.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Emflaza	deflazacort susp	22.75 MG/ML	M ; N ; O ; Y	N		
Emflaza	deflazacort tab	18 MG ; 30 MG ; 36 MG ; 6 MG	M ; N ; O ; Y	O ; Y		
Agamree	vamorolone oral susp	40 MG/ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Agamree	vamorolone oral susp	40 MG/ML	3	Bottles	30	DAYS			
Emflaza	Deflazacort Tab 18 MG	18 MG	30	Tablets	30	DAYS			
Emflaza	Deflazacort Tab 6 MG	6 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Agamree	vamorolone oral susp	40 MG/ML	Medicaid
Emflaza	deflazacort susp	22.75 MG/ML	Medicaid
Emflaza	deflazacort tab	18 MG ; 30 MG ; 36 MG ; 6 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Agamree	vamorolone oral susp	40 MG/ML	Medicaid
Emflaza	Deflazacort Tab 18 MG	18 MG	Medicaid
Emflaza	Deflazacort Tab 6 MG	6 MG	Medicaid

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PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. The patient has been treated with the requested agent (starting on samples is not approvable) with the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. ALL of the following: 1. ONE of the following: A. The patient has a diagnosis of Duchenne Muscular Dystrophy confirmed by genetic analysis (i.e., dystrophin deletion or duplication mutation) (genetic test required) **OR** B. The patient has another FDA labeled indication for the requested agent and route of administration **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for the use of the requested agent for the patient's age for the requested indication **AND** 3. ONE of the following: A. The patient's medication history includes generic prednisone (or prednisolone) AND ONE of the following: 1. The patient has had an inadequate response generic prednisone (or prednisolone) **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over generic prednisone (or prednisolone) **OR** B. The prescriber has provided information that the patient has an intolerance or hypersensitivity to generic prednisone (or prednisolone) that is NOT expected to occur with the requested agent **OR** C. The patient has an FDA labeled contraindication to generic prednisone (or prednisolone) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that generic prednisone (or prednisolone) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND**

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Module	Clinical Criteria for Approval
	2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pediatric neurologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 4. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose based on the patient's weight **Length of Approval:** 6 months for Agamree, 12 months for Emflaza NOTE: If Quantity Limit applies, please refer to Quantity Limit criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [NOTE: Patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had improvements or stabilization with the requested agent (e.g., slowed disease progression, improved strength, timed motor function, pulmonary function; reduced need for scoliosis surgery) **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pediatric neurologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose based on the patient's weight **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested agent strength does not have a program quantity limit **OR** 3. The request agent is Emflaza and ONE of the following: A. The requested agent is Emflaza SUSPENSION **OR** B. BOTH of the following: 1. The requested quantity (dose) exceeds the program quantity limit **AND** 2. The requested quantity (dose) cannot be achieved with a lower quantity of any combination of the four Emflaza tablet strengths **OR** 4. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Approval Length:** up to 12 months

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